Appendix D – Effectiveness evidence

Study	Dietary supplements for chronic gout (Cochrane review) trial: Andrés 2014[2]
Study type	Systematic Review
Number of studies (number of participants)	2 (n=160)
Countries and setting	Conducted in New Zealand; Setting: Rheumatology clinic/ Unclear
Line of therapy	Unclear
Duration of study	Intervention + follow up: average 10 weeks (3months and 8 weeks)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: American College of Rheumatology diagnostic classification/ preliminary criteria
Stratum	Overall
Subgroup analysis within study	Not applicable: subgroup analysis was reported for whether or not patients were allopurinol naive.
Inclusion criteria	Cochrane review protocol: Types of studies: RCTs, quasi-RCTs (clinical controlled trials, CCTS) that compare dietary supplements with no supplements, placebo, another supplement or pharmacological agents for chronic gout were considered for inclusion. Only trials that were publishes as full articles or available as a full trial report were included. Types of participants: adults ages 18 years or older with a diagnosis of chronic gout. Interventions: trials were included evaluating any dietary supplement including, but not limited to, amino acids, antioxidants, PUFAs, prebiotics, vitamins, alone or in combination. All doses and administration routes were examined. Comparators could have been: placebo, no treatment, a different dietary supplement, pharmacological therapy, non-pharmacological therapy or combination therapy.

Exclusion criteria	Trials in acute gout where the aims of treatment were different, namely to reduce acute inflammation, studies that incorporated a mix of people with gout and other musculoskeletal diseases unless the results of the people with gout could be separated out for analysis.
Recruitment/selection of patients	Dalbeth: Patients were recruited from rheumatology clinics and by public advertisement. Stamp: not reported
Age, gender and ethnicity	Age - Other: Dalbeth mean (SD): 57 (16), Stamp: mean (range): 61.2 (39-86). Gender (M:F): Dalbeth: (M:F): 108/12; Stamp: (M:F): 36/4. Ethnicity: Dalbeth: Caucasian: Lactose group 70%, SMP 70% ,SMP/GMP/G600 55% Overall: 58% Caucasian Stamp: New Zealand European 15 (37.5%), Other 25(62.5%)
Further population details	1. BMI: Systematic review: mixed (Dalbeth:BMI: Not stated / Unclear, Stamp: BMI: BMI 30 or over (obese)). 2. CKD stage : Mixed population (people with CKD and people without CKD) (Dalbeth: CKD stage: Not stated / Unclear; Stamp: CKD stage : People with CKD (stages 1-2)).
Indirectness of population	No indirectness
Interventions	(n=80) Intervention 1: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. SMP/ lactose. Duration 3 months. Concurrent medication/care: none reported. Indirectness: No indirectness Further details: 1. Setting: Systematic review: mixed Comments: SMP and lactose group combined for analysis. (n=40) Intervention 2: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. SMP enriched with GMP and G600 (GMP protein 1.5g (10% total protein) and G600 0.525g (3.5% of total protein weight). Duration 3 months. Concurrent medication/care: none reported. Indirectness: No indirectness Further details: 1. Setting: Systematic review: mixed (n=10) Intervention 3: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. vitamin C 500mg daily. Duration 8 weeks. Concurrent medication/care: None reported. Indirectness: No indirectness Further details: 1. Setting: Systematic review: mixed Comments: People not taking allopurinol at baseline

	(n=10) Intervention 4: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. Allopurinol 50-100mg daily (dose adjustment at 4 weeks based on sUA level). Duration 8 weeks. Concurrent medication/care: None reported. Indirectness: No indirectness Further details: 1. Setting: Systematic review: mixed Comments: People not taking allopurinol at entry (n=10) Intervention 5: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. Vitamin C 500mg daily(added to stable dose of allopurinol). Duration 8 weeks. Concurrent medication/care: Stable dose of allopurinol. Indirectness: No indirectness Further details: 1. Setting: Systematic review: mixed Comments: People taking allopurinol at baseline (n=10) Intervention 6: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. Allopurinol 50-100mg daily (increased the allopurinol dose, no specified dose scheme). Duration 8 weeks. Concurrent medication/care: None reported. Indirectness: No indirectness Further details: 1. Setting: Systematic review: mixed Comments: People taking allopurinol at baseline
Funding	Other (Dalbeth 2012 was funded by LactoPharma (a joint venture between Fonterra Ld, Fonterra R&D Ltd and Auckland UniServices Ltd) and the New Zealand government Foundation for Research science and Technology. Barbara Kuhn-Sherlock, Alastair MAcGibbonand Kate Palamo are employees of Fonterra Co-operative group Ltd. AlastairMacGibbon, Nicola Dalbeth and KAte Palamo are named inventors on a patent application related to milk products and gout, although it says that 'data analysis was completed by a biostatistician independent of the study sponsors'. Stamp was independent research carried out with no relation to vitamin C or allopurinol producers.
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SMP/ GMP/ G600 versus SMP/ LACTOSE (CONTROL) Protocol outcome 1: Quality of life medium-term (3 to 12 months) - Actual outcome: HAQ-II Physical function at 3 months; Group 1: mean 0.08 (SD 0.23); n=35, Group 2: mean 0.11 (SD 0.319); n=69; Health assessment questionnaire (HAQ-II) 0-3 Top=High is poor outcome	

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: Dalbeth study was blinded, Stamp was open-label.; Group 1 Number missing: 5, Reason: unclear; Group 2 Number missing: 11, Reason: unclear

Protocol outcome 2: Pain short-term medium-term (3 to 12 months)
- Actual outcome: Pain during gout flares at 3 months; Group 1: mean -1.97 (SD 2.28); n=40, Group 2: mean -0.94 (SD 2.25); n=-80; Likert scale 0-10 Top=High is poor outcome
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: Dalbeth study was blinded, Stamp was open-label.; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: Frequency of flares medium-term (3 to 12 months)
- Actual outcome: Number of gout flares per month at After 3 months; Group 1: mean 0.4928 (SD 1.52); n=40, Group 2: mean 0.7 (SD 1.28); n=80
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: Dalbeth study was blinded, Stamp was open-label.; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 4: Proportion of participants who reach serum urate target level medium-term (3 to 12 months)
- Actual outcome: Serum urate reduction at 3 months; Group 1: mean 0.0248 (SD 0.0668); n=33, Group 2: mean -0.01 (SD 0.0686); n=69
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: Dalbeth study was blinded, Stamp was open-label.; Group 1 Number missing: 7; Group 2 Number missing: 11

Protocol outcome 5: Total adverse events (3 to 12 months)
- Actual outcome: Withdrawal due to adverse events at 3 months; Group 1: 7/40, Group 2: 11/80
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: Dalbeth study was blinded, Stamp was open-label.; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: VITAMIN C 500MG DAILY (PEOPLE NOT ALREADY TAKING ALLOPURINOL) versus ALLOPURINOL 50-100MG DAILY (PEOPLE NOT ALREADY TAKING ALLOPURINOL)

Protocol outcome 1: Proportion of participants who reach serum urate target level medium-term (3 to 12 months)
- Actual outcome: Serum urate reduction at 8 weeks; Group 1: mean -0.004 (SD 0.0791); n=10, Group 2: mean -0.15 (SD 0.0791); n=10
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Not reported in risk of bias; Blinding details: Dalbeth study was blinded, Stamp was open-

label.; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: VITAMIN C 500MG DAILY (PEOPLE ALREADY TAKING ALLOPURINOL) versus ALLOPURINOL 50-100MG DAILY (PEOPLE ALREADY TAKING ALLOPURINOL)

Protocol outcome 1: Proportion of participants who reach serum urate target level short-term (less than 3 months)
- Actual outcome: Serum urate reduction at 8 weeks; Group 1: mean -0.03 (SD 0.0759); n=10, Group 2: mean -0.09 (SD 0.0791); n=10
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: Dalbeth study was blinded, Stamp was open-label.; Group 1 Number missing: 0; Group 2 Number missing: 0

ROBIS quality assessment of systematic reviews

Study eligibility criteria: low concerns

Identification and selection of studies: low concerns

Data collection and study appraisal: low concerns

Synthesis and findings: low concerns

Risk of bias in the review: low concerns

Protocol outcomes not reported by the study	Quality of life short-term (less than three months) at Define; Quality of life Long-term (more than 12 months) at Define; Pain short-term (less than 3 months) at Define; Pain short-term Long-term (more than 12 months) at Define; Joint swelling/inflammation short-term (less than 3 months) at Define; Joint swelling/inflammation medium-term (3 to 12 months) at Define; Joint swelling/inflammation long-term (more than 12 months) at Define; Joint tenderness short-term (less than 3 months) at Define; Joint tenderness medium-term (3 to 12 months) at Define; Joint tenderness long-term (more than 12 months) at Define; Frequency of flares short-term (less than 3 months) at Define; Frequency of flares long-term (more than 12 months) at Define; Patient global assessment of treatment success short-term (less than three months) at Define; Patient global assessment of treatment success medium-term (3 to 12 months) at Define; Patient global assessment of treatment success long-term (more than 12 months) at Define; Proportion of participants who reach serum urate target level long-term (more than 12 months) at Define; Radiographic joint damage (less than 3 months) at Define; Radiographic joint damage (3 to 12 months) at Define; Radiographic joint damage (more than 12 months) at Define; Renal stones (less than 3 months) at Define; Renal stones (3 to 12 months) at Define; Renal stones (more than 12 months) at Define; Tophi short-term (less than 3 months) at Define; Total adverse events (less than 3 months) at Define; Tophi

	medium-term (3 to 12 months) at Define; Tophi long-term (more than 12 months) at Define; Admissions (hospital and A&E/urgent care) short-term (less than 3 months) at Define; Admissions (hospital and A&E/urgent care) medium-term (3 to 12 months) at Define; Admissions (hospital and A&E/urgent care) long-term (more than 12 months) at Define; GP visits short-term (less than 3 months) at Define; GP visits medium-term (3 to 12 months) at Define; GP visits long-term (more than 12 months) at Define; Total adverse events (more than 12 months) at Define

Study	**Dalbeth 2012[10]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=120)
Countries and setting	Conducted in New Zealand; Setting: Patients were recruited from rheumatology clinics and by public advertisement in Auckland, New Zealand from July 2009 to June 2010 (final study visit October 2010).
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: diagnosis of gout according to the American College of Rheumatology diagnostic classification
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients were aged ≥18 years old, had a diagnosis of gout (according to the American College of Rheumatology diagnostic classification) and were experiencing frequent gout flares at the time of study enrolment (at least two flares in the preceding 4 months).

Exclusion criteria	Lactose intolerance and severe renal impairment (estimated glomerular filtration rate (eGFR) <30 ml/min). One hundred and thirty-one patients were screened.
Age, gender and ethnicity	Age - Mean (SD): Lactose group: 56 (17), SMP: 56 (12), SMP/GMP/G600: 56 (13). Gender (M:F): 108/12. Ethnicity: Caucasian: Lactose group 70%, SMP 70% , SMP/GMP/G600 55%
Further population details	1. BMI: Not stated / Unclear 2. CKD stage: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=40) Intervention 1: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. Lactose powder. Each intervention was a cream-coloured powder administered daily as a 250 ml vanilla flavoured shake mixed in water by the patient using a wand blender. The lactose content of the lactose powder control was chosen to parallel the amount found in the SMP study products. Duration 3 months. Concurrent medication/care: Qualifying participants entered a 1-month run-in phase during which all completed a gout flare diary. Those returning a completed diary proceeded to randomisation. Medication use at baseline, n(%): allopurinol 21 (53%), colchicine 12 (30%), prednisolone 4 (10%), NSAID 11 (28%), diuretic 2 (5%). Indirectness: No indirectness. Further details: 1. Setting: Not applicable (tertiary medical centre). (n=40) Intervention 2: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. Skim milk powder (SMP). The amount of SMP used in the SMP formulations was adjusted to give a total protein content of 15 g. Duration 3 months. Concurrent medication/care: Qualifying participants entered a 1-month run-in phase during which all completed a gout flare diary. Those returning a completed diary proceeded to randomisation. Medication use at baseline: allopurinol 22(55%), colchicine 7 (18%), prednisolone 8 (20%), NSAID 10(25%), diuretic 1 (2.5%). Indirectness: No indirectness. Further details: 1. Setting: Not applicable (Tertiary medical centre). (n=40) Intervention 3: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. Skim milk powder (SMP) enriched with glycomacropeptide (GMP) and milk fat extract (G600) (1.5 g GMP protein (10% total protein) and 0.525 g G600 (3.5% of total protein weight)). Duration 3 months. Concurrent medication/care: Qualifying participants entered a 1-month run-in phase during which all completed a gout flare diary. Those returning a completed diary proceeded to randomisation.

	Medication use at baseline: allopurinol 22 (55%), colchicine 13 (33%), prednisolone 4 (10%), NSAID 11 (28%), diuretic 8 (20%). Indirectness: No indirectness. Further details: 1. Setting: Not applicable (Tertiary medical centre).
Funding	Study funded by industry (Funding was provided by LactoPharma (a joint venture between Fonterram Ltd, Fonterra R&D Ltd and Auckland UniServices Ltd) and the New Zealand Government Foundation for Research Science and Technology.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIETARY SUPPLEMENTATION E.G. ENRICHED SKIMMED MILK POWDER, CHERRY EXTRACT/CONCENTRATE, OMEGA-3 POLYUNSATURATED FATTY ACIDS, VITAMIN C versus DIETARY SUPPLEMENTATION E.G. ENRICHED SKIMMED MILK POWDER, CHERRY EXTRACT/CONCENTRATE, OMEGA-3 POLYUNSATURATED FATTY ACIDS, VITAMIN C

Protocol outcome 1: Total adverse events (3 to 12 months)
- Actual outcome: total adverse events at 3 months; Group 1: 19/40, Group 2: 20/40
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIETARY SUPPLEMENTATION E.G. ENRICHED SKIMMED MILK POWDER, CHERRY EXTRACT/CONCENTRATE, OMEGA-3 POLYUNSATURATED FATTY ACIDS, VITAMIN C versus DIETARY SUPPLEMENTATION E.G. ENRICHED SKIMMED MILK POWDER, CHERRY EXTRACT/CONCENTRATE, OMEGA-3 POLYUNSATURATED FATTY ACIDS, VITAMIN C

Protocol outcome 1: Total adverse events (3 to 12 months) - Actual outcome: total adverse events at 3 months; Group 1: 19/40, Group 2: 19/40
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0 ; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIETARY SUPPLEMENTATION E.G. ENRICHED SKIMMED MILK POWDER, CHERRY EXTRACT/CONCENTRATE, OMEGA-3 POLYUNSATURATED FATTY ACIDS, VITAMIN C versus DIETARY SUPPLEMENTATION E.G. ENRICHED SKIMMED MILK POWDER, CHERRY EXTRACT/CONCENTRATE, OMEGA-3 POLYUNSATURATED FATTY ACIDS, VITAMIN C

Protocol outcome 1: Total adverse events (3 to 12 months)
- Actual outcome: total adverse events at 3 months; Group 1: 20/40, Group 2: 19/40
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcomes not reported by the study	Quality of life in short-term (less than three months); Quality of life in medium-term (3 to 12 months); Quality of life in long-term (more than 12 months); Pain in short-term (less than 3 months); Pain in short-term medium-term (3 to 12 months); Pain in short-term and long-term (more than 12 months); Joint swelling/inflammation in short-term (less than 3 months); Joint swelling/inflammation in medium-term (3 to 12 months); Joint swelling/inflammation in long-term (more than 12 months); Joint tenderness in short-term (less than 3 months); Joint tenderness in medium-term (3 to 12 months); Joint tenderness in long-term (more than 12 months); Frequency of flares in short-term (less than 3 months); Frequency of flares in medium-term (3 to 12 months; Frequency of flares in long-term (more than 12 months); Patient global assessment of treatment success short-term (less than three months); Patient global assessment of treatment success medium-term (3 to 12 months); Patient global assessment of treatment success long-term (more than 12 months); Proportion of participants who reach serum urate target level short-term (less than 3 months); Proportion of participants who reach serum urate target level in medium-term (3 to 12 months); Proportion of participants who reach serum urate target level in long-term (more than 12 months); Radiographic joint damage (less than 3 months); Radiographic joint damage (3 to 12 months); Radiographic joint damage (more than 12 months); Renal stones (less than 3 months); Renal stones (3 to 12 months); Renal stones (more than 12 months); Tophi in short-term (less than 3 months); Total adverse events (less than 3 months); Tophi in medium-term (3 to 12 months); Tophi in long-term (more than 12 months); Admissions (hospital and A&E/urgent care) in short-term (less than 3 months); Admissions (hospital and A&E/urgent care) in medium-term (3 to 12 months); Admissions (hospital and A&E/urgent care) in long-term (more than 12 months); GP visits in short-term (less than 3 months); GP visits in medium-term (3 to 12 months); GP visits in long-term (more than 12 months); Total adverse events (more than 12 months)

Study	**Holland 2015[14]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=30)
Countries and setting	Conducted in Australia; Setting: Patients were recruited from the outpatient departments of the Royal prince Alfred and Concord Repatriation General Hospitals
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: American college of rheumatology criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Males and females aged >18 years with history of gout as per American College of Rheumatology criteria, who were on stable dose of urate lowering therapy at target (serum urate <0.36 mmol/L), were included in the study
Exclusion criteria	Patients were excluded from the study if they were unable to communicate in English (both verbal and written, to standardise information)
Age, gender and ethnicity	Age - Median (range): Intervention group 64 (44-80), Control group 61 (38-77). Gender (M:F): 27/2. Ethnicity: not reported
Further population details	1. BMI: BMI 25 or over (overweight) (intervention 29 (23 - 35), 30 (24 - 37)). 2. CKD stage: Mixed population (people with CKD and people without CKD) (CKD: intervention group 5 (33%), control group 5(33%)).
Indirectness of population	No indirectness

Interventions	(n=14) Intervention 1: Dietary modifications - Change in dietary patterns e.g. DASH, Mediterranean diets, dietary pattern based on gout management guidelines. Comprehensive dietary advice. In addition to the advice given to control group, the intervention group received dietary advice in line with British Society for Rheumatology guidelines for the management of gout. the advice recommended: (1) reducing red meat intake, and avoiding offal, shellfish and yeast extract; and (2) including low fat dairy products, vegetables and cherries and the potential benefit of coffee and vitamin C. Duration 6 months. Concurrent medication/care: Allopurinol dose, mean (range) (mg) - 415 (200-900)mg. Indirectness: No indirectness Further details: 1. Setting: Hospital/secondary (secondary). (n=15) Intervention 2: Dietary modifications - Change in dietary patterns e.g. DASH, Mediterranean diets, dietary pattern based on gout management guidelines. The control group received advice regarding the importance of compliance with drug therapy, the benefit of weight loss and exercise (achieve ideal body weight) and the benefit of reduced alcohol intake. They were also advised on target urate concentration. Duration 6 months. Concurrent medication/care: Allopurinol dose at baseline, mean (range) (mg) - 525 (100-900). Indirectness: No indirectness. Further details: 1. Setting: Hospital/secondary (secondary).
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CHANGE IN DIETARY PATTERNS E.G. DASH, MEDITERRANEAN DIETS, DIETARY PATTERN BASED ON GOUT MANAGEMENT GUIDELINES versus CHANGE IN DIETARY PATTERNS E.G. DASH, MEDITERRANEAN DIETS, DIETARY PATTERN BASED ON GOUT MANAGEMENT GUIDELINES

Protocol outcome 1: Frequency of flares in medium-term (3 to 12 months)
- Actual outcome: Flares at 6 months; Group 1: 2/14, Group 2: 1/15
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - study reports that one patient was excluded during the study due to development of tumour lysis and two dropped out. unclear how many missing in each group. study also states that 30 patients were randomised however baseline details are only reported for 29 patients; Indirectness of outcome: No indirectness; Group 1 Number missing: unclear; Group 2 Number missing: unclear

Protocol outcome 2: Proportion of participants who reach serum urate target level in medium-term (3 to 12 months)
- Actual outcome: Serum urate level (change score) at 6 months; Group 1: mean 0.3 mmol/L (SD 0.08); n=14, Group 2: mean 0.27 mmol/L (SD 0.07); n=15
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - study reports that one patient was excluded during the study due to development of tumour lysis and two dropped out. unclear how many missing in each group. study also states that 30 patients were randomised however baseline details are only reported for 29 patients; Indirectness of outcome: No indirectness; Group 1 Number missing: unclear; Group 2 Number missing: unclear

Protocol outcomes not reported by the study	Quality of life in short-term (less than three months); Quality of life in medium-term (3 to 12 months); Quality of life in long-term (more than 12 months); Pain in short-term (less than 3 months); Pain in short-term medium-term (3 to 12 months); Pain in short-term and long-term (more than 12 months); Joint swelling/inflammation in short-term (less than 3 months; Joint swelling/inflammation in medium-term (3 to 12 months); Joint swelling/inflammation in long-term (more than 12 months); Joint tenderness in short-term (less than 3 months); Joint tenderness in medium-term (3 to 12 months); Joint tenderness in long-term (more than 12 months); Frequency of flares in short-term (less than 3 months); Frequency of flares in long-term (more than 12 months); Patient global assessment of treatment success in short-term (less than three months); Patient global assessment of treatment success in medium-term (3 to 12 months); Patient global assessment of treatment success in long-term (more than 12 months); Proportion of participants who reach serum urate target level in short-term (less than 3 months); Proportion of participants who reach serum urate target level in long-term (more than 12 months); Radiographic joint damage (less than 3 months); Radiographic joint damage (3 to 12 months); Radiographic joint damage (more than 12 months); Renal stones (less than 3 months); Renal stones (3 to 12 months); Renal stones (more than 12 months); Tophi in short-term (less than 3 months); Total adverse events (less than 3 months); Tophi in medium-term (3 to 12 months); Tophi in long-term (more than 12 months); Admissions (hospital and A&E/urgent care) in short-term (less than 3 months); Admissions (hospital and A&E/urgent care) in medium-term (3 to 12 months); Admissions (hospital and A&E/urgent care) in long-term (more than 12 months); GP visits in short-term (less than 3 months); GP visits in medium-term (3 to 12 months); Total adverse events (3 to 12 months); GP visits in long-term (more than 12 months); Total adverse events (more than 12 months)

Study	**Juraschek 2021[17]**
Study type	RCT (Patient randomised; Crossover)

Number of studies (number of participants)	RCT (Patient randomised; Crossover)
Countries and setting	1 (n=43)
Line of therapy	Conducted in USA; Setting: primary care
Duration of study	Not applicable
Method of assessment of guideline condition	Intervention + follow up: 4 weeks
Stratum	Adequate method of assessment/diagnosis
Subgroup analysis within study	Overall
Inclusion criteria	Eligible participants were community-dwelling adults, aged ≥18 years, with a self-reported diagnosis of gout and a SU concentration ≥7 mg/dL. Gout was based on self-report in response to the question "Has a physician told you that you have gout?"
Exclusion criteria	Exclusion criteria included: active use of or plans for urate lowering therapy, excessive alcohol use, stage 4 or 5 chronic kidney disease, unstable medication use (steroid, lipid-lowering, or antihypertensive agents), active prescriptions of warfarin or insulin, major gastrointestinal conditions affecting food absorption, or inability to store food at home
Recruitment/selection of patients	Participants were recruited by identifying patients with a diagnosis of gout in the Johns Hopkins Medicine medical record, newspaper advertisements, Facebook advertisements, and mass mailings to adults living in the communities surrounding the research centre. After completion of two in-person visits at the Johns Hopkins ProHealth Clinical Research Unit (Woodlawn, Maryland, US.
Age, gender and ethnicity	Age - Mean (SD): 59/12.1. Gender (M/F): 35/8. Ethnicity: Not reported
Further population details	1. BMI: BMI 30 or over (obese) (33.5 (6.8)). 2. CKD stage: Mixed population (people with CKD and people without CKD) (eGFR, mL/min 1.73 mm2 = 78.7(16.1)).
Indirectness of population	No indirectness

Interventions	(n=22) Intervention 1: Dietary modifications - Change in dietary patterns e.g. DASH, Mediterranean diets, dietary pattern based on gout management guidelines. Dietitian directed DASH groceries - During the DDG intervention, participants participated in a one-on-one session with a dietitian at the initiation of the intervention, followed by weekly phone calls thereafter. The educational content of these sessions was restricted to instructions to eat the study foods and avoid non-study foods During the DDG assignment, participants were allotted a stipend of $105/week for the purchase of food (i.e., $15/day). We primarily used Amazon Fresh (Seattle, Washington, USA) to order and deliver foods to the ProHealth research centre for weekly pick-up by the participant. DASH diet 5–7 servings/day of grains, 4 servings/day of fruit, 4 servings/day of vegetables, 1–2 servings/day of lean meat (poultry/fish), 2 servings/day of low fat dairy, and <0.5 servings/day of high fibre foods (nuts, seeds, legumes). During the DDG period, participants were also asked to restrict alcohol, sugar-sweetened beverages (no soda, no juice), sweets, red meat, organ meats, and shellfish. Food orders were selected to be low in fat, saturated fat, and cholesterol, consistent with the original DASH diet. We also focused on groceries consistent with consuming less than 2300 mg of sodium a day. Duration 4 weeks. Concurrent medication/care: Diuretic use 27 %, losartan use 18%, Colchicine use 14%, NSAID's 14%. Indirectness: No indirectness. Further details: 1. Setting: Primary/community (n=21) Intervention 2: Dietary modifications - Change in dietary patterns e.g. DASH, Mediterranean diets, dietary pattern based on gout management guidelines. Self-directed groceries. Duration 4 weeks. Concurrent medication/care: Diuretic use 29 %, losartan use 24%, Colchicine use 19%, NSAID's 14%. Indirectness: No indirectness. Further details: 1. Setting: Primary/community (n=22) Intervention 3: Dietary modifications - Change in dietary patterns e.g. DASH, Mediterranean diets, dietary pattern based on gout management guidelines. Dietitian directed DASH groceries/Self-directed groceries - During the DDG intervention, participants participated in a one-on-one session with a dietitian at the initiation of the intervention, followed by weekly phone calls thereafter. The educational content of these sessions was restricted to instructions to eat the study foods and avoid non-study foods During the DDG assignment, participants were allotted a stipend of $105/week for the purchase of food (i.e., $15/day). We primarily used Amazon Fresh (Seattle, Washington, USA) to order and deliver foods to the ProHealth research centre for weekly pick-up by the participant. DASH diet 5–7 servings/day of grains, 4 servings/day of fruit, 4 servings/day of vegetables, 1–2 servings/day of lean meat (poultry/fish), 2 servings/day of low fat dairy, and <0.5 servings/day of high-fibre foods (nuts, seeds, legumes). During the DDG period, participants were also asked to restrict alcohol, sugar-sweetened beverages (no soda, no juice), sweets, red meat, organ meats, and shellfish. Food orders were selected to be low in fat, saturated fat, and cholesterol, consistent with the original DASH diet. We also focused on groceries consistent with consuming less than 2300 mg of sodium a day. After 4 weeks patients crossed over to self-directed groceries. Duration 8 weeks. Concurrent medication/care: Period 1 - Diuretic use 27 %, losartan use 18%, Colchicine use 14%, NSAID's 14%. period 2 not stated. Indirectness: No indirectness Further details: 1. Setting: Primary/community (n=21) Intervention 4: Dietary modifications - Change in dietary patterns e.g. DASH, Mediterranean diets, dietary pattern based

	on gout management guidelines. Self-directed groceries/Dietitian directed DASH groceries - after 4 weeks on self-directed groceries patients crossed over dietitian-directed groceries. During the DDG intervention, participants participated in a one-on-one session with a dietitian at the initiation of the intervention, followed by weekly phone calls thereafter. The educational content of these sessions was restricted to instructions to eat the study foods and avoid non-study foods During the DDG assignment, participants were allotted a stipend of $105/week for the purchase of food (i.e., $15/day). We primarily used Amazon Fresh (Seattle, Washington, USA) to order and deliver foods to the ProHealth research centre for weekly pick-up by the participant. DASH diet 5–7 servings/day of grains, 4 servings/day of fruit, 4 servings/day of vegetables, 1–2 servings/day of lean meat (poultry/fish), 2 servings/day of low fat dairy, and <0.5 servings/day of high fibre foods (nuts, seeds, legumes). During the DDG period, participants were also asked to restrict alcohol, sugar-sweetened beverages (no soda, no juice), sweets, red meat, organ meats, and shellfish. Food orders were selected to be low in fat, saturated fat, and cholesterol, consistent with the original DASH diet. We also focused on groceries consistent with consuming less than 2300 mg of sodium a day. Duration 8 weeks. Concurrent medication/care: Period 1: Diuretic use 29 %, losartan use 24%, Colchicine use 19%, NSAID's 14% Period 2 not reported. Indirectness: No indirectness Further details: 1. Setting: Primary/community Interventions 3 and 4 were not included as it was a cross-over study with no wash-out period, therefore there could be carry over from the previous interventions.
Funding	Academic or government funding (S.P.J. is supported by a NIH/NHLBI K23HL135273. DIGO was supported by a grant from the Rheumatology Research Foundation. K. A. Carson's work on the project was funded by the Johns Hopkins Institute for Clinical and Translational Research, under grant number UL1 TR003098 from the National Centre for Advancing Translational Sciences, a component of the National Institutes of Health (NIH) and the NIH Roadmap for Medical Research. HKC is supported by NIH grant P50AR060772

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CHANGE IN DIETARY PATTERNS E.G. DASH, MEDITERRANEAN DIETS, DIETARY PATTERN BASED ON GOUT MANAGEMENT GUIDELINES versus CHANGE IN DIETARY PATTERNS E.G. DASH, MEDITERRANEAN DIETS, DIETARY PATTERN BASED ON GOUT MANAGEMENT GUIDELINES

Protocol outcome 1: Proportion of participants who reach serum urate target level short-term (less than 3 months)

- Actual outcome: Serum urate level, change from baseline at 4 weeks; Group 1: mean -0.55 mg/dL (SD 1.16); n=22, Group 2: mean 0 mg/dL (SD 1.03); n=21

Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CHANGE IN DIETARY PATTERNS E.G. DASH, MEDITERRANEAN DIETS, DIETARY PATTERN BASED ON GOUT MANAGEMENT GUIDELINES versus CHANGE IN DIETARY PATTERNS E.G. DASH, MEDITERRANEAN DIETS, DIETARY PATTERN BASED ON GOUT MANAGEMENT GUIDELINES

Protocol outcome 1: Proportion of participants who reach serum urate target level short-term (less than 3 months)

- Actual outcome: Serum urate level, change from baseline at 8 weeks; Group 1: mean -0.48 mg/dL (SD 1.18); n=22, Group 2: mean -0.05 mg/dL (SD 1.01); n=21

Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - High; Indirectness of outcome: No indirectness; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcomes not reported by the study	Quality of life in short-term (less than three months); Quality of life medium-term (3 to 12 months); Quality of life in long-term (more than 12 months); Pain in short-term (less than 3 months); Pain in short-term and medium-term (3 to 12 months); Pain in short-term and long-term (more than 12 months); Joint swelling/inflammation in short-term (less than 3 months); Joint swelling/inflammation medium-term (3 to 12 months); Joint swelling/inflammation in long-term (more than 12 months); Joint tenderness short-term (less than 3 months); Joint tenderness in medium-term (3 to 12 months); Joint tenderness in long-term (more than 12 months); Frequency of flares in short-term (less than 3 months); Frequency of flares in medium-term (3 to 12 months); Frequency of flares in long-term (more than 12 months); Patient global assessment of treatment success in short-term (less than three months); Patient global assessment of treatment success in medium-term (3 to 12 months); Patient global assessment of treatment success in long-term (more than 12 months); Proportion of participants who reach serum urate target level in medium-term (3 to 12 months); Proportion of participants who reach serum urate target level in long-term (more than 12 months); Radiographic joint damage (less than 3 months); Radiographic joint damage (3 to 12 months); Radiographic joint damage (more than 12 months); Renal stones (less than 3 months); Renal stones (3 to 12 months); Renal stones (more than 12 months); Tophi short-term (less than 3 months); Total adverse events (less than 3 months); Tophi in medium-term (3 to 12 months); Tophi in long-term (more than 12 months); Admissions (hospital and A&E/urgent care) in short-term (less than 3 months); Admissions (hospital and A&E/urgent care) medium-term (3 to 12 months); Admissions (hospital and A&E/urgent care) in long-term (more than 12 months); GP visits in short-term (less than 3 months); GP visits in medium-term (3 to 12 months); Total adverse events (3 to 12 months); GP visits in long-term (more than 12 months); Total adverse events (more than 12 months)

Study (subsidiary papers)	**Schlesinger 2012[31]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=18)
Countries and setting	Conducted in USA; Setting: Unclear/not stated
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 4 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: MSU crystal- proven gout
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Eighteen patients with MSU crystal- proven gout were entered into this study.
Exclusion criteria	Not stated
Age, gender and ethnicity	Age - Median (range): 56.43 (28-75). Gender (M:F): not reported. Ethnicity: Caucasian 11, Asian 1, Hispanic 1, African American 1
Further population details	1. BMI: BMI 30 or over (obese) (mean (SE) - 30.02(0.84). 2. CKD stage: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=9) Intervention 1: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. Cherry juice - patients received a tablespoon of cherry juice concentrate twice daily. Duration 4 months. Concurrent medication/care: 3 of 9 patients (33%) were taking allopurinol

	(100-500 mg daily). Five patients (55%) in group A taking NSAIDs chronically (Celcoxib n=3; indomethacin n=2) discontinued NSAIDs within 60 days of starting cherry juice. Indirectness: No indirectness Further details: 1. Setting: Not stated / Unclear (n=5) Intervention 2: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. Pomegranate juice - patients received a tablespoon of pomegranate juice concentrate twice daily. Duration 4 months. Concurrent medication/care: 2 of 5 patients were taking allopurinol (100-500 mg daily). Indirectness: No indirectness Further details: 1. Setting: Not stated / Unclear
Funding	Equipment / drugs provided by industry (The prospective RCT was supported by a grant from Brownwood Acres Foods.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIETARY SUPPLEMENTATION E.G. ENRICHED SKIMMED MILK POWDER, CHERRY EXTRACT/CONCENTRATE, OMEGA-3 POLYUNSATURATED FATTY ACIDS, VITAMIN C versus DIETARY SUPPLEMENTATION E.G. ENRICHED SKIMMED MILK POWDER, CHERRY EXTRACT/CONCENTRATE, OMEGA-3 POLYUNSATURATED FATTY ACIDS, VITAMIN C

Protocol outcome 1: Frequency of flares medium-term (3 to 12 months)
- Actual outcome: Flares - number of flares at 4 months; Group 1: 7/9, Group 2: 6/5
Risk of bias: All domain - Low, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: Flares - number of people with at least 1 gout flare at 4 months; Group 1: 4/9, Group 2: 4/5
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0

Protocol outcome 2: Proportion of participants who reach serum urate target level medium-term (3 to 12 months)
- Actual outcome: serum urate level (mg/dL) at 4 months; Group 1: mean 8.17 mg/dL (SD 3.3); n=9, Group 2: mean 6.14 mg/dL (SD 2.39); n=5
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcomes not reported by the study	Quality of life in short-term (less than three months); Quality of life in medium-term (3 to 12 months); Quality of life in long-term (more than 12 months); Pain in short-term (less than 3 months); Pain in short-term and medium-term (3 to 12 months); Pain in short-term and long-term (more than 12 months); Joint swelling/inflammation in short-term (less than 3 months); Joint swelling/inflammation in medium-term (3 to 12 months); Joint swelling/inflammation in long-term (more than 12 months); Joint tenderness in short-term (less than 3 months); Joint tenderness in medium-term (3 to 12 months); Joint tenderness in

	long-term (more than 12 months); Frequency of flares in short-term (less than 3 months); Frequency of flares in long-term (more than 12 months); Patient global assessment of treatment success in short-term (less than three months); Patient global assessment of treatment success in medium-term (3 to 12 months); Patient global assessment of treatment success in long-term (more than 12 months; Proportion of participants who reach serum urate target level in short-term (less than 3 months); Proportion of participants who reach serum urate target level in long-term (more than 12 months); Radiographic joint damage (less than 3 months); Radiographic joint damage (3 to 12 months); Radiographic joint damage (more than 12 months); Renal stones (less than 3 months); Renal stones (3 to 12 months); Renal stones (more than 12 months); Tophi in short-term (less than 3 months); Total adverse events (less than 3 months); Tophi in medium-term (3 to 12 months); Tophi in long-term (more than 12 months); Admissions (hospital and A&E/urgent care) in short-term (less than 3 months); Admissions (hospital and A&E/urgent care) in medium-term (3 to 12 months); Admissions (hospital and A&E/urgent care) in long-term (more than 12 months); GP visits in short-term (less than 3 months); GP visits in medium-term (3 to 12 months); Total adverse events (3 to 12 months); GP visits in long-term (more than 12 months); Total adverse events (more than 12 months)

Study (subsidiary papers)	**Singh 2019[32] (Singh 2020[33])**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=84)
Countries and setting	Conducted in USA
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 9 months
Method of assessment of guideline condition	Unclear method of assessment/diagnosis: patient self-reported physician diagnosis of gout
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	(1) US adults aged 18 years or older; (2) a valid US mailing address and e-mail address; (3) patient self-reported physician diagnosis of gout.
Exclusion criteria	Self-reported presence of other types of inflammatory arthritis including rheumatoid arthritis or spondyloarthritis and the current use of cherry extract, juice, or concentrate.
Age, gender and ethnicity	Age - Mean (SD): Cherry extract group: 58.2 (15.5), Diet modification group: 53.6 (11.9). Gender (M:F): 61/23. Ethnicity: Cherry extract group: White 30 (73%), Black or African American 9 (22%), Asian/other/mixed 2 (5%); Diet modification group. White 27 (63%), Black or African American 12 (28%), Asian/other/mixed 4 (9%);
Further population details	1. BMI: Not stated / Unclear 2. CKD stage : Not stated / Unclear

Indirectness of population	No indirectness
Interventions	(n=41) Intervention 1: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. Cherry extract 3,600 mg daily (3 capsules of 1200 mg each daily, each equivalent to 32 oz of cherry juice or a pound of cherries. Patients were sent the 3-month supply of cherry capsules, to each study participant at 3, 6, and 9 months, supplemented with study coordinator calls to encourage cherry extract adherence. Receipt was confirmed via e-mail or phone conversation. Duration 9 months. Concurrent medication/care: Taking allopurinol, febuxostat or probenecid at baseline 13 (33%). Indirectness: No indirectness. Further details: 1. Setting: Not stated / Unclear (n=43) Intervention 2: Dietary modifications - Change in dietary patterns e.g. DASH, Mediterranean diets, dietary pattern based on gout management guidelines. Diet modification. Patients were sent individualized diet recommendation (based on baseline FFQ data) to each study participant at 3, 6, and 9 months, supplemented with dietitian calls to discuss specific recommendations. Receipt was confirmed via e-mail or phone conversation. Duration 9 months. Concurrent medication/care: Taking allopurinol, febuxostat or probenecid at baseline 17(42%). Indirectness: No indirectness. Further details: 1. Setting: Not stated / Unclear
Funding	Academic or government funding (This study was funded by an intramural grant from the University of Alabama at Birmingham Centre for Outcomes and Effectiveness Research and Education/Minority Health Research Centre (principal investigator, J.A.S.) and an intramural grant from the University of Alabama at Birmingham Centre for Clinical and Translational Studies (principal investigator, J.A.S.). The funding body did not play any role in the design, collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIETARY SUPPLEMENTATION E.G. ENRICHED SKIMMED MILK POWDER, CHERRY EXTRACT/CONCENTRATE, OMEGA-3 POLYUNSATURATED FATTY ACIDS, VITAMIN C versus CHANGE IN DIETARY PATTERNS E.G. DASH, MEDITERRANEAN DIETS, DIETARY PATTERN BASED ON GOUT MANAGEMENT GUIDELINES

Protocol outcome 1: Pain short-term in medium-term (3 to 12 months)
- Actual outcome: Pain - average pain score over 24 hours at 9 months; Group 1: mean 0.84 (SD 1.44); n=32, Group 2: mean 0.85 (SD 1.69); n=26
Risk of bias: All domain - Very high, Selection - Low, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9; Group 2 Number missing: 7

Protocol outcome 2: Frequency of flares medium-term (3 to 12 months)

	- Actual outcome: Flares (proportion with any gout flare patient reported) at 9 months; Group 1: 23/41, Group 2: 28/43 Risk of bias: All domain - Very high, Selection - Low, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing:0 ; Group 2 Number missing: 0 Protocol outcome 3: Patient global assessment of treatment success medium-term (3 to 12 months) - Actual outcome: HAQ-DI. (Health assessment questionnaire-disability index) at 9 months; Group 1: mean 0.28 (SD 0.54); n=41, Group 2: mean 0.23 (SD 0.4); n=42; Comments: 0-1 mild to moderate disability; 1-2 moderate to severe disability; 2-3 severe to very severe disability. Risk of bias: All domain - Very high, Selection - Low, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 4: Proportion of participants who reach serum urate target level medium-term (3 to 12 months) - Actual outcome: Serum urate level at 9 months; Group 1: mean 7.16 mg/dL (SD 1.71); n=41, Group 2: mean 7 mg/dL (SD 1.91); n=43 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome: Number of patients achieving sUA <6mg/dL at 9 months; Group 1: 7/34, Group 2: 8/31 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 7; Group 2 Number missing: 12 - Actual outcome: Number of patients achieving sUA <5mg/dL at 9 months; Group 1: 2/34, Group 2: 5/31 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 7; Group 2 Number missing: 12 Protocol outcome 5: Total adverse events (3 to 12 months) - Actual outcome: AE - Any adverse events at 9 months; Group 1: 1/32, Group 2: 0/26; Comments: reported as a percentage Cherry group 3.1 % N=32; Diet group 0.0% N=26. Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 9; Group 2 Number missing: 7 - Actual outcome: AE - specific gastrointestinal adverse events at 9 months; Group 1: 9/32, Group 2: 7/26; Comments: reported as a percentage Cherry group 28.1 % N=32; Diet group 26.9% N=26 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9; Group 2 Number missing: 7
Protocol outcomes not reported by the study	Quality of life in short-term (less than three months); Quality of life in medium-term (3 to 12 months); Quality of life in long-term (more than 12 months); Pain in short-term (less than 3 months); Pain short-term Long-term (more than 12 months); Joint swelling/inflammation in short-term (less than 3 months); Joint swelling/inflammation in medium-term (3 to 12 months); Joint swelling/inflammation in long-term (more than 12 months); Joint tenderness in short-term (less than 3 months); Joint

	tenderness in medium-term (3 to 12 months); Joint tenderness in long-term (more than 12 months); Frequency of flares in short-term (less than 3 months); Frequency of flares in long-term (more than 12 months); Patient global assessment of treatment success in short-term (less than three months); Patient global assessment of treatment success in long-term (more than 12 months); Proportion of participants who reach serum urate target level in short-term (less than 3 months); Proportion of participants who reach serum urate target level in long-term (more than 12 months); Radiographic joint damage (less than 3 months); Radiographic joint damage (3 to 12 months); Radiographic joint damage (more than 12 months); Renal stones (less than 3 months); Renal stones (3 to 12 months); Renal stones (more than 12 months); Tophi in short-term (less than 3 months); Total adverse events (less than 3 months); Tophi in medium-term (3 to 12 months); Tophi in long-term (more than 12 months); Admissions (hospital and A&E/urgent care) in short-term (less than 3 months); Admissions (hospital and A&E/urgent care) in medium-term (3 to 12 months); Admissions (hospital and A&E/urgent care) in long-term (more than 12 months); GP visits in short-term (less than 3 months); GP visits in medium-term (3 to 12 months); GP visits in long-term (more than 12 months); Total adverse events (more than 12 months)

Study	**Stamp 2013[35]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=20)
Countries and setting	Conducted in New Zealand; Setting: Unclear
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 8 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: American College of Rheumatology preliminary criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with gout, whose diagnosis was defined according to the American College of Rheumatology preliminary criteria and with an SU level >0.36 mmoles/liter (6 mg/dl) were recruited.
Exclusion criteria	Patients taking over-the-counter vitamin supplements were excluded
Age, gender and ethnicity	Age - Mean (range): Vit C group - 61.2(39-86), no vitamin C - 55(27 - 78). Gender (M:F): 36/4. Ethnicity: New Zealand European 15 (37.5%), Other 25(62.5%)
Further population details	1. BMI: BMI 30 or over (obese) (vitamin C (30.4(0.96), no vitamin C 32(1.5)). 2. CKD stage : People with CKD (stages 1-2)
Extra comments	None
Indirectness of population	No indirectness

Interventions	(n=10) Intervention 1: Dietary modifications - Increased intake of; coffee, dairy or vitamin C (dietary and supplementary) omega-3, Polyunsaturated Fatty Acids, rich fish, cherries, tomatoes, water. Vitamin C 500 mg per day (in patients not taking allopurinol at baseline). Duration 2 months. Concurrent medication/care: Patients not taking allopurinol at baseline. Indirectness: No indirectness. Further details: 1. Setting: Not stated / Unclear (n=10) Intervention 2: Urate-lowering medications - xanthine oxidase inhibitors. Allopurinol up to 100mg per day. Allopurinol was started at 50mg or 100mg (in patients not taking allopurinol at baseline). Duration 2 months. Concurrent medication/care: Patients not taking allopurinol at baseline. Indirectness: No indirectness. Further details: 1. Setting: Not stated / Unclear (n=10) Intervention 3: Dietary modifications - Increased intake of; coffee, dairy or vitamin C (dietary and supplementary)omega-3, Polyunsaturated Fatty Acids, rich fish, cherries, tomatoes, water. Vitamin C at a dosage of 500 mg/day (in patients already taking allopurinol at baseline). Duration 2 months. Concurrent medication/care: Patients already taking allopurinol at baseline. Indirectness: No indirectness. Further details: 1. Setting: Not stated / Unclear (n=10) Intervention 4: Urate-lowering medications - xanthine oxidase inhibitors. Allopurinol increased dose. Allopurinol was increased by 50 mg or 100mg increments, at the discretion of the physician, depending on each patient's renal function and comorbidities. The dose of allopurinol was further increased at 4 weeks if the patient had not achieved the target SU level of <0.36 mmoles/litre (6mg/dl). Duration 2 months. Concurrent medication/care: Patients already taking allopurinol at baseline. Indirectness: No indirectness. Further details: 1. Setting: Not stated / Unclear
Funding	Academic or government funding (Supported by the Health Research Council of New Zealand)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INCREASED INTAKE OF; COFFEE, DAIRY OR VITAMIN C (DIETARY AND SUPPLEMENTARY) OMEGA-3, POLYUNSATURATED FATTY ACIDS, RICH FISH, CHERRIES, TOMATOES, WATER versus XANTHINE OXIDASE INHIBITORS

Protocol outcome 1: Proportion of participants who reach serum urate target level short-term (less than 3 months)
- Actual outcome: Serum urate level (in people not taking allopurinol at baseline) at 2 months; Group 1: mean -0.07 (SD 1.26); n=10, Group 2: mean -2.5 (SD 1.26); n=10
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;
Indirectness of outcome: No indirectness; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INCREASED INTAKE OF; COFFEE, DAIRY OR VITAMIN C (DIETARY AND SUPPLEMENTARY) OMEGA-3, POLYUNSATURATED FATTY ACIDS, RICH FISH, CHERRIES, TOMATOES, WATER. versus XANTHINE OXIDASE INHIBITORS

Protocol outcome 1: Proportion of participants who reach serum urate target level short-term (less than 3 months) - Actual outcome: Serum urate level (in people already taking allopurinol at baseline) at 2 months; Group 1: mean -0.5 (SD 1.26); n=10, Group 2: mean -1.5 (SD 1.26); n=10 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing:0 ; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Quality of life in short-term (less than three months); Quality of life in medium-term (3 to 12 months); Quality of life in long-term (more than 12 months); Pain in short-term (less than 3 months); Pain in medium-term (3 to 12 months); Pain in long-term (more than 12 months); Joint swelling/inflammation in short-term (less than 3 months); Joint swelling/inflammation medium-term (3 to 12 months); Joint swelling/inflammation in long-term (more than 12 months); Joint tenderness in short-term (less than 3 months); Joint tenderness in medium-term (3 to 12 months); Joint tenderness in long-term (more than 12 months); Frequency of flares in short-term (less than 3 months); Frequency of flares in medium-term (3 to 12 months); Frequency of flares in long-term (more than 12 months); Patient global assessment of treatment success in short-term (less than three months); Patient global assessment of treatment success in medium-term (3 to 12 months); Patient global assessment of treatment success in long-term (more than 12 months); Proportion of participants who reach serum urate target level in medium-term (3 to 12 months); Proportion of participants who reach serum urate target level in long-term (more than 12 months); Radiographic joint damage (less than 3 months); Radiographic joint damage (3 to 12 months); Radiographic joint damage (more than 12 months); Renal stones (less than 3 months); Renal stones (3 to 12 months); Renal stones (more than 12 months); Tophi in short-term (less than 3 months); Total adverse events (less than 3 months); Tophi in medium-term (3 to 12 months); Tophi in long-term (more than 12 months); Admissions (hospital and A&E/urgent care) in short-term (less than 3 months); Admissions (hospital and A&E/urgent care) in medium-term (3 to 12 months); Admissions (hospital and A&E/urgent care) in long-term (more than 12 months); GP visits in short-term (less than 3 months); GP visits in medium-term (3 to 12 months); Total adverse events (3 to 12 months); GP visits in long-term (more than 12 months); Total adverse events (more than 12 months)

Study	**Stamp 2020[34]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=50)
Countries and setting	Conducted in New Zealand; Setting: Not reported.

Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 28 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with gout as defined by the ARA preliminary classification criteria for gout with a SU of >0.36 mmol/l (6 mg/dl) were recruited.
Exclusion criteria	People with type 1 diabetes and those receiving diuretics were excluded.
Recruitment/selection of patients	Recruitment was selective to ensure half the participants were receiving allopurinol and half were on no ULT.
Age, gender and ethnicity	Age - Mean (SD): Placebo group: 56.9(12.9) 7.5ml group: 63.3 (13.0), 15ml group: 61.0 (9), 22.5ml group: 56.2 (11.4), 30ml group: 60.4 (11.6). Gender (M:F): Placebo group: 9M/1F 7.5ml group: 9M/1F, 15ml group: 9M/1F, 22.5ml group: 8M/2F, 30ml group: 10M/0F. Ethnicity: Placebo group: NZ European 4, Maori/ Pacific 6; 7.5ml group: NZ European 9, Maori/ Pacific 1 15ml group: NZ European 7, Maori/ Pacific 3; 22.5ml group: NZ European 7, Maori/ Pacific 3; 30ml group: NZ European 8, Maori/ Pacific 2
Further population details	1. BMI: Systematic review: mixed (Placebo group: 30.5(9.2) 7.5ml group: 31.2(10.0), 15ml group: 28.8(3.7), 22.5ml group: 28.9 (3.2), 30ml group: 29.5(4.5)). 2. CKD stage : Mixed population (people with CKD and people without CKD) (Placebo group: 2, 7.5ml group: 0, 15ml group: 0, 22.5ml group: 0, 30ml group: 1).
Indirectness of population	No indirectness
Interventions	(n=10) Intervention 1: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. 7.5 ml of tart cherry juice concentrate twice daily in 250ml water for 28 days. Participants were provided with cherry concentrate 946ml bottles, which contain juice from about 3000 Montmorency cherries (1 ml about 3 cherries) and about 15g sugar per 30 mls). Duration 28 days. Concurrent medication/care: 5 patients were taking allopurinol. Indirectness: No indirectness. Further details: 1. Setting: Not stated /

	Unclear (n=10) Intervention 2: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. 15 ml of tart cherry juice concentrate twice daily in 250ml water for 28 days. Participants were provided with Cherry Concentrate 946ml bottles, which contain juice from about 3000 Montmorency cherries (1 ml about 3 cherries) and about 15g sugar per 30 mls). Duration 28 days. Concurrent medication/care: 5 patients were taking allopurinol. Indirectness: No indirectness. Further details: 1. Setting: Not stated / Unclear (n=10) Intervention 3: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. 22.5 ml of tart cherry juice concentrate twice daily in 250ml water for 28 days. Participants were provided with cherry concentrate 946ml bottles, which contain juice from about 3000 Montmorency cherries (1 ml about 3 cherries) and about 15g sugar per 30 mls). Duration 28 days. Concurrent medication/care: 5 patients were taking allopurinol. Indirectness: No indirectness. Further details: 1. Setting: Not stated / Unclear (n=10) Intervention 4: Dietary modifications - Dietary supplementation e.g. enriched skimmed milk powder, cherry extract/concentrate, Omega-3 Polyunsaturated Fatty Acids, vitamin C. 30 ml of tart cherry juice concentrate twice daily in 250ml water for 28 days. Participants were provided with cherry concentrate 946ml bottles, which contain juice from about 3000 Montmorency cherries (1 ml about 3 cherries) and about 15g sugar per 30 mls). Duration 28 days. Concurrent medication/care: 5 patients were taking allopurinol. Indirectness: No indirectness. Further details: 1. Setting: Not stated / Unclear (n=10) Intervention 5: Placebo - e.g. with some dietary supplement studies. 2 drops of tart cherry juice concentrate twice daily in 250ml water for 28 days. Participants were provided with cherry concentrate 946ml bottles, which contain juice from about 3000 Montmorency cherries (1 ml about 3 cherries) and about 15g sugar per 30 mls). Duration 28 days. Concurrent medication/care: 5 patients were taking allopurinol. Indirectness: No indirectness. Further details: 1. Setting: Not stated/Unclear
Funding	Academic or government funding (Heath Research Council of New Zealand).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 7.5ML CHERRY EXTRACT/CONCENTRATE versus PLACEBO Protocol outcome 1: Frequency of flares in short-term (less than 3 months)	

- Actual outcome: Gout flares at Day 28; Group 1: mean 0.6 (SD 0.5); n=10, Group 2: mean 0.4 (SD 0.5); n=10
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Proportion of participants who reach serum urate target level in short-term (less than 3 months)
- Actual outcome: Serum urate (mmol/l) at Day 28; Group 1: mean 0.4 (SD 0.08); n=10, Group 2: mean 0.47 (SD 0.12); n=10
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: Total adverse events (less than 3 months)
- Actual outcome: Adverse events. at within the 28 day study period; Group 1: 3/10, Group 2: 6/10
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 4: Admissions (hospital and A&E/urgent care) in short-term (less than 3 months)
- Actual outcome: Serious adverse events (Hospital admission with a condition deemed unrelated to study medication.) at within the 28 day study period; Group 1: 2/10, Group 2: 0/10; Comments: 1 patient was admitted to hospital after requiring surgery for a strangulated hernia on day 7. 1 patient was admitted to hospital with an exacerbation of heart failure on day 21. Possible double counting with the adverse events outcome.
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 15ML CHERRY EXTRACT/CONCENTRATE versus PLACEBO

Protocol outcome 1: Frequency of flares in short-term (less than 3 months)
- Actual outcome: Gout flares at Day 28; Group 1: mean 0.4 (SD 0.5); n=10, Group 2: mean 0.4 (SD 0.5); n=10
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Proportion of participants who reach serum urate target level in short-term (less than 3 months)
- Actual outcome: Serum urate (mmol/l) at Day 28; Group 1: mean 0.44 (SD 0.1); n=10, Group 2: mean 0.47 (SD 0.12); n=10
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: Total adverse events (less than 3 months)
- Actual outcome: Adverse events. at within the 28 day study period; Group 1: 11/10, Group 2: 6/10; Comments: There were 24 adverse events in 24 patients during the study. The number in the cherry group appears to be incorrect.

Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 22.5ML CHERRY EXTRACT/CONCENTRATE versus PLACEBO

Protocol outcome 1: Frequency of flares short-term (less than 3 months)
- Actual outcome: Gout flares at Day 28; Group 1: mean 0.6 (SD 0.5); n=10, Group 2: mean 0.4 (SD 0.5); n=10
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing:

Protocol outcome 2: Proportion of participants who reach serum urate target level short-term (less than 3 months)
- Actual outcome: Serum urate (mmol/l) at Day 28; Group 1: mean 0.44 (SD 0.12); n=10, Group 2: mean 0.47 (SD 0.12); n=10
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: Total adverse events (less than 3 months)
- Actual outcome: Adverse events. at within the 28 day study period; Group 1: 2/10, Group 2: 2/10
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 30ML CHERRY EXTRACT/CONCENTRATE versus PLACEBO

Protocol outcome 1: Frequency of flares in short-term (less than 3 months)
- Actual outcome: Gout flares at Day 28; Group 1: mean 0.4 (SD 0.5); n=10, Group 2: mean 0.4 (SD 0.5); n=10
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Proportion of participants who reach serum urate target level in short-term (less than 3 months)
- Actual outcome: Serum urate (mmol/l) at Day 28; Group 1: mean 0.42 (SD 0.08); n=10, Group 2: mean 0.47 (SD 0.12); n=10
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Total adverse events (less than 3 months)
- Actual outcome: Adverse events. at within the 28 day study period; Group 1: 2/10, Group 2: 2/10
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low,

Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Quality of life in short-term (less than three months); Quality of life in medium-term (3 to 12 months); Quality of life in long-term (more than 12 months); Pain in short-term (less than 3 months); Pain in medium-term (3 to 12 months); Pain in long-term (more than 12 months); Joint swelling/inflammation in short-term (less than 3 months); Joint swelling/inflammation in medium-term (3 to 12 months); Joint swelling/inflammation in long-term (more than 12 months); Joint tenderness in short-term (less than 3 months); Joint tenderness in medium-term (3 to 12 months); Joint tenderness in long-term (more than 12 months); Frequency of flares in medium-term (3 to 12 months); Frequency of flares in long-term (more than 12 months); Patient global assessment of treatment success in short-term (less than three months); Patient global assessment of treatment success in medium-term (3 to 12 months); Patient global assessment of treatment success in long-term (more than 12 months); Proportion of participants who reach serum urate target level in medium-term (3 to 12 months); Proportion of participants who reach serum urate target level in long-term (more than 12 months); Radiographic joint damage (less than 3 months); Radiographic joint damage (3 to 12 months); Radiographic joint damage (more than 12 months); Renal stones (less than 3 months); Renal stones (3 to 12 months); Renal stones (more than 12 months); Tophi short-term (less than 3 months); Tophi in medium-term (3 to 12 months); Tophi in long-term (more than 12 months); Admissions (hospital and A&E/urgent care) in medium-term (3 to 12 months); Admissions (hospital and A&E/urgent care) long-term (more than 12 months); GP visits short-term (less than 3 months); GP visits in medium-term (3 to 12 months); Total adverse events (3 to 12 months); GP visits long-term (more than 12 months); Total adverse events (more than 12 months)